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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,110	11/05/2001	Lillian E Dyck	10242 34	3978

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BERESKIN AND PARR
SCOTIA PLAZA
40 KING STREET WEST-SUITE 4000 BOX 401
TORONTO, ON M5H 3Y2
CANADA

EXAMINER	
REYES, HECTOR M	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,110	DYCK ET AL.	
	Examiner	Art Unit	
	Hector M Reyes	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/19/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16; 24-31* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☒ Claim(s) *15* is/are allowed.

6)☒ Claim(s) *1-6,8-14,16 and 25-31* is/are rejected.

7)☒ Claim(s) *7,11 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election

Examiner acknowledges Applicant's election with traverse of Group I, in Paper dated April 19, 2004. The said group I consists of Claims 1-10, 11-16 and 25-31, in part, drawn to a series of compounds of Formula I wherein X is a carboxylic acid; compositions comprising the said derivatives and Method of treatment or prevention a particular disease described in claim 30.

The traversal is on the grounds that:

- "It is believed that all of the compounds of Formula I can be searched without undue burden on the Office"

This is not found persuasive because the inventions listed as Groups I through VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

- Inventions outlined above are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions 1-VIII are different because they are not disclosed as capable of using together. For instance, the claimed method of use and pharmaceutical compositions are not required to use all the compounds from each one of the above groups. On the other hand, compounds embrace in one Group are not required to be used in the method of

use or pharmaceutical compositions of compounds of another group. Similarly, a commercial package is not required to treat a any of the diseases embraced in the other groups, while the diseases included in claim 30 are not the only diseases embraced by groups I through VI.

- These inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.
- Clearly the search required for any of the above groups is not required for the other Groups, restriction for examination purposes as indicated is proper.
- Each one of the above Inventions are different from each other because a given reference anticipating or suggesting one of the inventions under the meaning of 35 USC 102 or 35 USC 103, respectively, cannot be used to reject any of the other invention under 35 USC 102 or 35 USC 103.

The requirement is still deemed proper and is therefore made FINAL.

Status of The Claims

Claims 17-23 have been canceled. Claims 8-10, 16 and 24 have been amended. Currently, Claims 1-10, 11-16 and 25-31, in part, drawn to a series of compounds of Formula I wherein X is a carboxylic acid; compositions comprising the said derivatives and Method of treatment or prevention a particular disease described in claim 30 are under Examination.

Claim Objections-Multiple dependency

Claims 11 and 12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple depend claims. The said claims depend on claims 3-9 and claim 6 is a multiple depending claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The embodiment of a method for the **prevention** of a disease in which cell death occurs by apoptosis in Claims 25-31 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. Elements of the said prevention method would requires:

- Identification of all diseases embraced by the said "disease in which cell death occurs by apoptosis"
- A clear process for identification of all subjects that would suffer any of the said diseases with a high degree of accuracy
- A process, including the right age, time and conditions for the subject to receive the "effective amount of the said compound"
- Showing that the subjects already treated would never suffer from any of the multiple diseases embraced by the term "cell death by apoptosis".

The said elements are critical or essential to the practice of the invention, however are not included in the claims and not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Without the proper identification of subjects that certainly would suffer a given condition or disease, and further identification of conditions of treatment and follow up of the said group of individuals for a long period of time cannot exist a prevention of a given disease.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of some disease in which cell death occurs by apoptosis using some compounds, ***does not reasonably provide enablement for the treatment of <u>any disease</u> in which cell death occurs by apoptosis using <u>other</u> compounds embraced by the said claims.*** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands* 8 USPQ2d 1400 (1988) , factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 101, first paragraph have been described. They are:

1. the nature of the invention

2. the state of the Prior art
3. the predictability or lack thereof in the art
4. amount of direction or guidance in the specification
5. working Examples in the specification
6. the breadth of the claims
7. the quantity of experimentation
8.the level of one skilled in the art.

Some of the factors considered in the above determination are:

The nature of the invention

The nature of the invention is the treatment of all disease in which cell death occurs by apoptosis such as stroke, head trauma, Bell's palsy, spinal cord injury, Alzheimer's disease, Parkinson's disease, Pick's disease, amyotrophic lateral sclerosis, Huntington's disease, multiple sclerosis, cardiac myopathies, nephropaty, retinophathy, diabetic complications, glaucoma and idiopathic neuropathies (Claim 30).

Moreover, the nature of the invention -effective treatment of a given disease- requires a rational wherein the nature of the chemical structure is quite relevant in the biological interaction bases. It is very unlikely that substances with a considerable difference in their structure and with a variety of functional groups would all be effective in the same treatment.

The state of the Prior art and the predictability or lack thereof in the art

The state of the prior art is that involve screening in vitro and in vivo to determine which compounds embraced by formula (I) exhibit the desired biological activity . There is no absolute predictability even considering a person highly skilled in the art, thus, the more unpredictability, the more specific enablement is needed in order to satisfy the statute.

In the instant case, there are some data in vitro supporting the enablement for some compounds but not in others, see page 17 and 18.

The breadth of the claims

Applicants claims a method for the treatment of any disease in which cell death occurs by apoptosis comprising the administration of an affective amount of a compound of formula I.

Thus, the said method would include conditions that may be related to cell death by apoptosis in the future, without not even being tested. Regarding the number of compounds embraced in Formula (I), there are many organic compounds that would satisfy the limitations of the said formula.

Examples provided in the Specification

On page 18 there are a series of results containing biological data demonstrating the effectiveness of some carboxylic acid derivatives in the said method of treatment. However some of the results indicate that there is no "rescue". Therefore, some of the compounds embraced by Formula I in claim 25 are indeed not active in the said treatment.

Thus, a person skill in the art would need to carry out extensive experimentation in order to develop a method for the treatment of all diseases in which cell death occurs by apoptosis such as stroke, head trauma, Bell's palsy, spinal cord injury, Alzheimer's disease, Parkinson's disease, Pick's disease, amyotrophic lateral sclerosis, Huntington's disease, multiple sclerosis, cardiac myopathies, nephropaty, retinophathy,

diabetic complications, glaucoma and idiopathic neuropathies and by using the multiple compounds embraced by formula (I).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 3-6, 16 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 are indefinite because while the chirality of the claimed compounds is included s a limitation, there is no indication where is the chiral carbon in the claimed compound. Moreover, considering that the said chiral carbon atom is the one wherein R1-R3 are connected, the definition of the compound includes instances wherein the said carbon atom may have two substituents that are the same. For instance, the said definition embraces instances wherein R2 is a methyl group and wherein m is 0, thus R1 is also a methyl group. Which is the chiral carbon atom in the claimed compounds?

Claim 5 recites the limitation "A compound of Formula I according to claim 1". There is insufficient antecedent basis for this limitation in the claim. Claim 1 does not exclude some compounds, as described in claim 5. It is unclear why claim 5 excludes some of the compounds embraces by claim 1. If claim 5 depends on claim 1 then it also should

includes all limitations of claim 1. Are compounds excluded from claim 5 known compounds? Why are they included in claim 1 but excluded in claim 5?

Claim 6 recites the limitation "a compound according to any one of claims 1 to 5". There is insufficient antecedent basis for this limitation in the claim. In claim 6, the description of the claimed compounds is different from the compounds described in claims 1-5. Indeed the said definition is a lot broader, since the said substituents on R1 are not included in the prior claims 1-5.

In claim 16 the phrase "a composition according to claim 11 is indefinite and confusing since claim 11 is not drawn to a composition if not to a compound.

In claim 25, the term "A method for the treatment or prevention of a disease in which cell death occurs by apoptosis" is indefinite. The said phrase is a ***"reach through claim***". What are the said diseases intended to be treated or prevented? Is this method directed to unknown diseases that may be related to cell death by apoptosis in the future? Moreover, the said claim is also indefinite because it includes a method for "prevention" of the said general condition. How the said condition can be prevented?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5; 9-12, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipate by Morris-Sherwood et al, US patent 4548726 (1985).

Morris-Sherwood discloses 2-methylheptyl aminopropionic acid as an amphoteric surfactant, see column 1, lines 29-35. Morris-Sherwood also discloses compositions comprising the said derivatives, see column 1, lines 40-67 and column II, lines 1-26 and examples given.

Claims 1, 2, 5, 9-12 and 13-14 are rejected under 35 USC 102 (b) as being anticipated by Dudzinski et al, US patent 3991208 (1976).

Dudzinski discloses a series of amphoteric surface-active substance, which are derivatives of propionic acid having an amine derivative ant the third position of the said acid or its corresponding salt, see for instance, column 1, lines 18-34. Dudzinski also discloses compositions comprising the said compounds, see for instance column 3, lines 5-13 and examples.

Claims 1 and 8 are rejected under 35 USC 102 (b) as being anticipated by Tien et al, JACS, 1955, vol. 77 pages 6696-6698.

Tien discloses the preparation of the hydrochlorides of glycine N-hexyl, see page 6697.

Claims 1 is rejected under 35 USC 102 (b) as being anticipated by many references, among them:

- CA 1998:45464: Hamper et al, Journal of Organic Chemistry, vol. 63 (3) (1998) pages 708-718. Hamper discloses, beta alanine, N-dodecyl with registry number 1462-54-0, beta alanine, N-(1-methylethyl) with registry number 16217-35-9,

beta alanine, N-(methyl propyl) with registry number 202059-85-6 and other species embraced by claim 1

- CA 1996:637648 US Patents 5565290 and 5723239 discloses beta alanine, N-hexyl and beta alanine, N-(2-ethylhexyl)- with registry number 101816-76-6
- CA 1995:878827, WO 9512610 discloses Glycine, N-hexyl registry number 41331-10-6
- CA 1993:46312, Nakamura et al, Colloids and Surfaces (1992) vol. 67, pages 183-193 discloses beta alalnine, N-hexyl, registry number 41331-11-7; beta alanine, N-butyl with registry number 77390-89-7; beta alanine, N-octyl registry number 27373-57-5, among others
- CA 1992:59021, Bulletin of the Korean Chemical Society, 1991, vol. 12(5) page 589, discloses beta alanine, N-1-methylethyl)- with registry number 16217-35-9
- CA 1991:27105 US patent 4961873 discloses Glycine, N- (1,1-dimethylethyl)- registry number 58482-93-2
- CA 1989:38631, ES patent 2003836 discloses beta alanine, N-octadecyl with registry number 112-87-8 and beta alanine N-(9Z)-9-octadecenyl with registry number 41331-11-7
- CA 1987:440328 US patent 4804500, discloses Glycine, N-(1-methylethyl) 3183-21-9 and glycine, N-methyl-N-(1-methylethyl) with registry number 108957-96-6.

Claim Objections

Claim 7 is objected because the said claim depends on rejected claim 3.

Allowable Subject Matter

Compositions described in instant claim 15 were not found disclosed or suggested in the prior art.

CONCLUSION

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. International Search Report for PCT Application PCT/CA/99/00250 is hereby incorporated as well as all references included in the said report. Applicant's attention is drawn to the fact that extensive list of references disclosing compounds embraced in the instant claims were found in the prior art, particularly by claim 1 and that the mention or used of all the references would be impractical.

Any inquiry concerning this communication should be directed to Hector M. Reyes whose telephone number is (571) 272-0691. The examiner can normally be reached on Monday to Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner 's supervisor, Ms. Rita Desai can be reached on (571) 272-0684. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556 or for regular communication and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Hector M. Reyes PhD JD
AU 1625
June 16, 2004

R. Desai
6/18/04